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EXAMINER
ROYDS, LESLIE A

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,059	ARTERBURN ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *10-13 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,14,15 and 21* is/are rejected.

7)☒ Claim(s) *3-6,10-13 and 16-20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *19 May 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are presented for examination.

Applicant's claim for priority under 35 U.S.C. 119(e) from provisional application number 60/413,857 filed September 27, 2002 is acknowledged. Applicant's Information Disclosure Statement filed May 19, 2004 has been received and entered into the application. As reflected by the attached, completed copy of substituted form PTO-1449A (4 pages total), the Examiner has considered the cited references.

Claim Objection for Improper Multiple Dependency

Claims 10-13 and 16-20 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). **Accordingly, claims 10-13 and 16-20 have not been further treated on the merits.**

Claim Objections-Minor Informalities

Claim 5 is objected to for failing to refer back to the patient recited in previous claims 1, 2, 3 or 4 as ---said patient--- rather than "a patient" in line 2 of the claim. Appropriate correction is required for consistency of the claims.

Claims 3 and 6 are objected to because of the following informalities:

(i) the word "mellitus" is misspelled at line 1 of claim 3; and

(ii) the word "antiplatelet" is misspelled at line 1 of claim 6.

Appropriate correction is required.

Claim 4 is objected to for failing to define the acronym "CRP" at its first occurrence in the claims. Claim 4 should be rewritten to read ---C-reactive protein (CRP)--- at line 2 of the claim. Appropriate correction is required.

Specification

The Examiner has noted the incorporation by reference of International Patent Publications WO 02/11564 at page 4, paragraph [011], line 13, WO 02/02105 at page 5, paragraph [013], line 13 and WO 94/28913 at page 11, paragraph [034], line 2 of the disclosure. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. See 37 C.F.R. 1.57(f). Applicant is required to amend any improper incorporation by reference of essential subject matter, as the above-cited locations may not reflect all the places at which improper incorporation by reference occurs in the present specification.

The disclosure is objected to because of the following informalities:

(i) the word "stroke" is misspelled at page 8, paragraph [025], line 3 and at page 9, paragraph [027], line 3; and

(ii) the phrase "…a clinical trial a population…" at page 23, paragraph [075], line 1 of the disclosure should be corrected to read "…a clinical trial **of** a population…" for clarity.

Appropriate correction is required.

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-9 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of a disease associated with subclinical inflammation, does not reasonably provide enablement for preventing the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;

2) the breadth of the claims;

3) the predictability or unpredictability of the art;

4) the amount of direction or guidance presented;

5) the presence or absence of working examples;

6) the quantity of experimentation necessary;

7) the state of the prior art; and,

8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation. The Examiner has noted the variety of conditions to which Applicant has claimed invention using the claimed active agent. For the purposes of consideration under 35 U.S.C. 112, first paragraph, the Examiner has focused on the specific subclinical inflammatory condition of hypertension. However, the reasons stated here concerning the burden of enabling the prevention of hypertension apply also to the other above-mentioned conditions, but for the obvious difference in the type of disorder.

Factors 1 and 2) The claimed invention is directed to the use of docosahexaenoic acid (DHA) to a patient in an amount effective to reduce subclinical inflammation (defined by Applicant at page 1, paragraph [0003], line 1 as "chronic non-acute systemic inflammation") to impede the development or progression of a disease associated with subclinical inflammation (see present claim 1). Exemplary conditions associated with subclinical inflammation recited in the present claims include cerebrovascular disease, coronary artery disease, peripheral artery

disease, type 2 diabetes mellitus, metabolic syndrome or hypertension (see present claims 2-3). Also provided is a method of prophylactic therapy for subclinical inflammation comprising the administration of DHA to a patient with an elevated level of circulating C-reactive protein (see present claim 4). DHA may be administered in conjunction with an antiplatelet agent, especially aspirin (see present claims 6-9 and 21).

Factor 3) There is a known unpredictability in the art when engaging in the prevention of hypertension, since the etiology of the condition is not known but has been suggested to be related, in part, to heredity, although the mechanism by which that occurs is unclear. The Merck Manual of Diagnosis and Therapy (Sixteenth Edition) notes, "…it seems improbable that a single cause will explain its diverse hemodynamic and pathophysiologic derangements" (Ch.24, p.413, second paragraph from the bottom of the page). Pharmacologic therapies, such as thiazide and related sulfonamide diuretics, loop diuretics, potassium-sparing diuretics, beta blockers, angiotensin converting enzyme inhibitors, calcium antagonists, adrenergic inhibiting agents and behavioral modifications, such as weight loss, restricted alcohol consumption and regular moderate exercise (see The Merck Manual, p.419 "Nonpharmacologic Therapy"), are known in the art to treat the symptoms associated with hypertension. Conventional therapies used for the treatment of hypertension are used to ameliorate and control the symptoms associated with the condition. However, the art does not recognize any type of therapeutic modality to cure or prevent such a condition, primarily because the etiology and risk factors associated with the development of hypertension are elusive and not particularly well characterized (see The Merck Manual, p. 413 and 419-426).

Factor 4) Applicant has merely disclosed that by administering the claimed active composition in a patient with hypertension, one may treat or prevent such a condition in a patient. Based on the discussion in Section 3 above, however, such disclosure clearly is not adequate direction or guidance as to how the proposed active agent(s) could be employed to accomplish the prevention of hypertension in a predictable manner.

Factor 5) The specification at page 9, paragraph [027], for example, discloses that use of the presently claimed active composition has activity in the treatment of hypertension in patients. Although Applicant discloses that prevention may be achieved, in the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing hypertension or how a patient could be kept from ever developing this condition. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active agent for the prevention of such a condition.

The Examiner acknowledges that the Office does not require the presence of working examples to be present in the disclosure of the invention (see MPEP §2164.02). However, in light of the state of the art, which recognizes particular conventional therapies, such as thiazide and related sulfonamide diuretics, loop diuretics, potassium-sparing diuretics, beta blockers, angiotensin converting enzyme inhibitors, calcium antagonists, adrenergic inhibiting agents and behavioral modifications, (See Factor 7, below), effective in the treatment of hypertension, the Office would require appropriate disclosure to support the contention that the use of the claim

specified active composition could actually prevent hypertension or the symptoms associated with such a condition by simply administering, by any method, an amount of the claimed active composition, especially in light of the fact that the present specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing such a condition using the claimed active composition.

Factor 6) The burden of enabling the prevention of hypertension is much greater than that of enabling the treatment of the same condition. Since the present specification would not enable the skilled artisan to prevent hypertension, a clear burden of undue experimentation would be placed upon the skilled artisan in order to practice this aspect of the invention.

Factor 7) Conventional therapies used to treat and control the conditions and symptoms associated with hypertension, such as thiazide and related sulfonamide diuretics, loop diuretics, potassium-sparing diuretics, beta blockers, angiotensin converting enzyme inhibitors, calcium antagonists, adrenergic inhibiting agents and behavioral modifications (see The Merck Manual, p. 413 and 419-426) are well known in the art as treatments for ameliorating the symptoms associated with hypertension. The use of these conventional therapies in patients experiencing hypertension is well known in the art, but is not recognized to have any curative, preventive or prophylactic effect against the development, advancement or cure of such a disease (see Section 3, above). Furthermore, it is more difficult to prevent the development or advancement of hypertension than it is to simply ameliorate the symptoms associated with the condition,

especially since it is recognized in the art that there is no known therapeutic modality for the prevention of such a condition.

Furthermore, the burden of enabling the prevention of **any** of the conditions recited in the present claims would be much greater than that of enabling the treatment of such conditions. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of prevention of such conditions or how a patient could be kept from ever developing these diseases. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active compound for the prevention of such conditions.

Specifically, it is highly unlikely, and the Office would require experimental evidence to support the contention, that the claim specified active composition could actually prevent the development of such conditions by simply administering, by any method, an amount of the claim specified composition. The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing the development of such conditions.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Since absolute success is not reasonably possible with most conditions, especially those having etiologies and pathophysiological manifestations that are as complex and/or poorly understood as the conditions recited in the present claims, the specification is viewed as lacking an adequate written description of how any of the above-mentioned conditions may be actually prevented.

Factor 8) In view of the discussion of each of the preceding seven factors, the level of skill in this art is high and is at least that of a medical doctor with several years of experience in the art.

Summary

As the cited art and discussion of the above 8 factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation that the prevention of hypertension could be achieved. In order to actually achieve prevention of this condition, it is clear from the discussion above that the skilled artisan could not rely on Applicant's disclosure as required by 35 U.S.C. §112, first paragraph. Given that the art fails to recognize and Applicant has failed to demonstrate that hypertension could actually be prevented, the skilled artisan would be faced with the impermissible burden of undue experimentation in order to practice this embodiment of the claimed invention. Accordingly, claims 4-9 and 21 are deemed properly rejected.

Suggestion for Overcoming the Rejection

In order to overcome the present rejection, Applicant may wish to consider amending the claims in the following manner. Claim 4 is provided below:

---4. A method of ~~prophylactic therapy~~ treatment for subclinical inflammation comprising administering an effective amount of DHA substantially contemporaneous with a second medicament to a patient, wherein said DHA and said second medicament are administered in an amount sufficient to reduce circulating C reactive protein in the patient.---

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

I Claims 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The MPEP sets forth the following:

"The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what Applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph, with respect to the claimed invention." (See MPEP §2173).

The term "about" in the expression "greater than about 750 mg/day" (see present claim 14) is a relative term that renders the claim indefinite. The expression "about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and, thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Use of the term "about" would invite subjective interpretations of whether or not a particular dosage amount is included or excluded from the present claims, and, thus, it is the Examiner's position that the public would not be informed of the boundaries of what constitutes infringement of the present claims. Such subjective determinations are inconsistent with the tenor and express requirements of 35 U.S.C. 112, second paragraph. Furthermore, it is not clear

whether "greater than" or "about" is meant to be the limiting term of the claim. The phrase "greater than" indicates that the dose may be any dose greater than 750 mg/day, but the term "about" indicates that the dose may be slightly above or below 750 mg/day. Claims 14 and 15 are, therefore, considered properly rejected.

II Claims 4-5 and 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

In light of the guidance of MPEP §2173, which emphasizes the requirement of definiteness of claim language, the term "reduce" in the expression "in an amount sufficient to reduce circulating CTP in the patient" (see claim 4, for example), the term "small" in the expression "small LDL particle size" (see claim 14, for example) and the term "elevated" in the expression "with elevated levels of C-reactive protein" (see claim 14, for example) are relative terms that render the claims indefinite. The expressions are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and, thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Use of the terms "reduce", "small" and "elevated" would invite subjective interpretations as to what degree the level of CRP would need to have decreased and the standard against which reduction is to be measured, what LDL particle size would be considered small and what level of CRP is considered to be elevated and the standard against which such an elevation is to be measured. Thus, it is the Examiner's position that the public would not be informed of the boundaries of what constitutes infringement of the present claims. Such subjective determinations are

inconsistent with the tenor and express requirements of 35 U.S.C. 112, second paragraph, and claims 4-5 and 14-15 are, therefore, considered properly rejected.

III Claims 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Claim 14 recites the steps of assessing an individual suspected to be at risk for stroke and subsequently providing an amount of DHA to be administered, but does not recite the step of identifying those individuals suspected of being at risk for stroke after the assessment process in order to identify the appropriate population of individuals to whom a dosage of DHA is to be provided and administered. Thus, claim 14, and also claim 15, due to its dependency on claim 14, is properly rejected under 35 U.S.C. 112, second paragraph, for claiming an incomplete method of treatment.

Examiner's Assessment of the Scope and Content of the Instant Claims

Claims 10-13 and 16-20 have not been further treated on the merits due to improper multiple dependency. Claims 1-9, 14-15 and 21 have been examined on the merits. Claim 4 is rejected above under 35 U.S.C. 112, first paragraph, and art will not be applied towards this claim under 35 U.S.C. 102 or 35 U.S.C. 103 because it lacks enablement. Claim 5 is recognized as a multiple dependent claim, dependent on any one of claims 1, 2, 3 or 4 and examination of this claim has been performed insofar as claim 5 reads upon claims 1, 2 or 3.

Legal Standard for Anticipation/Inherency Under - 35 USC § 102

To anticipate a claim under 35 U.S.C. 102, a single prior art reference must place the invention in the public's possession by disclosing each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to practice the invention. *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1001 (Fed. Cir. 1991); *In re Donahue*, 766 F.2d 531, 533, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). In order to anticipate, the prior art must either expressly or inherently disclose every limitation of the claimed invention. *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365, 52 U.S.P.Q.2d 1303, 1303 (Fed. Cir. 1999) (citing to *In re Schreiber*, 128 F.3d 1473, 1477, 44 U.S.P.Q.1429, 1431 (Fed. Cir. 1997)); *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 U.S.P.Q.2d 1943, 1946 (Fed. Cir. 1999). In order to inherently anticipate, the prior art must necessarily function in accordance with, or include, the claimed limitations. *MEHL/Biophile*, 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. However, it is not required that those of ordinary skill in the art recognize the inherent characteristics or the function of the prior art. *Id.* Specifically, discovery of the mechanism underlying a known process does not make it patentable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Zigerlig (UK Patent Application GB2218904A; 1989). Zigerlig teaches a highly purified pharmaceutical formulation of docosahexaenoic acid (DHA) in combination with a second antioxidant composition, such as tocopherol (see abstract, for example). Zigerlig also teaches the therapeutic applicability of DHA in the following conditions: atherosclerosis, prevention of thrombus formation, aortal and coronary arteriosclerosis, diabetes mellitus, cardiac infarction, platelet agglutination, hypertension, cerebral infarction and acute and chronic inflammation (page 8, line 11-page 9, line 8).

Although Zigerlig does not expressly teach coronary artery disease or peripheral artery disease, the reference does teach conditions such as atherosclerosis, aortal and coronary arteriosclerosis and cardiac infarction. Applicant has disclosed in the present specification that the object of the invention is to "...reduce subclinical inflammation in individuals who are at risk for developing, or who currently have, atherosclerotic cardiovascular disease, coronary disease..." (see Applicant's acknowledgement, page 6, paragraph [014]). The Examiner has used the guidance in the present specification to interpret the terms "coronary artery disease or peripheral artery disease" to read on atherosclerotic disease or any coronary disease. Thus, because Zigerlig discloses the use of DHA in atherosclerosis, coronary arteriosclerosis and cardiac infarction, it is found to directly anticipate the claim limitations of "coronary artery disease or peripheral artery disease" in present claim 2. Cerebral infarction is known in the art to be a cerebrovascular disease associated with embolism or thrombosis of intra- or extracranial arteries (see The Merck Manual of Diagnosis and Therapy, 16th Edition, 2001; p.1450), which is

considered by the Examiner to directly anticipate the claim limitation of cerebrovascular disease as recited in present claim 2. In concurrence with MPEP §2131.01, it is proper to rely on another reference for a rejection under 35 U.S.C. 102, provided that the additional reference is relied upon in order to explain the meaning of a term used in the primary reference.

Furthermore, Zigerlig discloses the use of highly purified DHA in treating diabetes mellitus, but does not expressly disclose the treatment of type 2 diabetes mellitus. However, although the reference discloses the genus of disorders known generally as diabetes mellitus, the number of species (eg, type 1 or type 2 diabetes mellitus; See The Merck Manual of Diagnosis and Therapy, 16th Edition, 2001; p.1107-9 and Table 91-1) is sufficiently small that the teachings of Zigerlig places the treatment of the disease type 2 diabetes mellitus using DHA well within the possession of the public and is, thus, considered to be anticipated and properly rejected under 35 U.S.C. 102(b). See *In re Schaumann*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978). See MPEP §2131.02 and §2144.08 for more information on anticipation and obviousness of species by a disclosure of a genus.

Rejection of Claim 5 Based on Inherency

It is recognized that the prior art teachings of Zigerlig do not expressly recite that the use of DHA administered with a second medicament, in this case, tocopherol, to reduce subclinical inflammation associated with cerebrovascular disease, coronary artery disease, peripheral artery disease, type II diabetes mellitus, metabolic syndrome or hypertension is given in an amount sufficient to reduce circulating C reactive protein in the patient, but the reference does, however,

teach a method of treating atherosclerosis, prevention of thrombus formation, aortal and coronary arteriosclerosis, diabetes mellitus, cardiac infarction, platelet agglutination, hypertension, cerebral infarction and acute and chronic inflammation (page 8, line 11-page 9, line 8). However, because the particular method steps and compounds that are present in the instant claims are also in the patent, it is deemed that the C reactive protein reduction properties of the amount of the compound of the prior art used to treat the above-mentioned conditions would have been inherent, whether recognized by the patentees or not. The claiming of a new use, new function or **unknown property** that is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 U.S.P.Q. 430, 433 (CCPA 1977). See also MPEP §2112. It is irrelevant that the prior art observers did not recognize the property or function of the disputed claims; if the prior art inherently possesses that characteristic, it anticipates. Applicant's attention is further drawn to the MPEP at §2113, which states, "As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). Thus, claims 1-3 and 5 are properly rejected as being anticipated by Zigerlig.

II Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Klor (European Patent Application 0843972A1; 1996). Klor teaches the use of polyunsaturated fatty acids, such as docosahexaenoic acid, in the treatment of metabolic syndrome (otherwise known as syndrome X, see abstract, for example).

It is recognized that the prior art teachings of Klor do not expressly recite the reduction of the subclinical inflammation associated with metabolic syndrome, but the reference does, however, teach a method of treating metabolic syndrome using DHA (see abstract, for example). However, because the particular method steps and compounds that are present in the instant claims are also in the patent, it is deemed that the reduction of any inflammation associated with the condition of metabolic syndrome using DHA would have been inherent, whether recognized by the patentees or not. The claiming of a new use, new function or **unknown property** that is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 U.S.P.Q. 430, 433 (CCPA 1977). See also MPEP §2112. It is irrelevant that the prior art observers did not recognize the property or function of the disputed claims; if the prior art inherently possesses that characteristic, it anticipates. Applicant's attention is further drawn to the MPEP at §2113, which states, "As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). Thus, claim 1 and 3 are properly rejected as being anticipated by Klor.

III Claims 1-2 and 5-9 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Serhan et al. (International Publication No. WO 01/60778 A2; 2001). Serhan et al. teaches a method of treating inflammation in a mammal by the administration of a combination of an omega-3 fatty acid, specifically, eicosapentanoic acid (EPA) or DHA, and aspirin (page 11, lines 15-16). Serhan et al. disclose that the method of treatment may be employed in the following

therapeutic uses: arterial inflammation, arthritis, cardiovascular diseases (page 11, lines 18-20), spasmogenic conditions, such as cerebral spasm or stroke (page 22, lines 18-25), conditions involving blood platelet aggregation, such as thrombosis, strokes having a total or partial thrombotic origin or coronary thrombosis (page 22, line 30-page 23, line 2), and inflammatory conditions of the heart, such as coronary infarct damage or smooth muscle proliferation disorders, such as restenosis following angioplasty (page 23, lines 22-25). Serhan et al. further teaches that DHA and aspirin may be administered at different times (page 11, lines 16-18), and in a therapeutically effective amount, described as "an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic results, e.g., a diminishment or prevention of inflammation associated with various disease states or conditions" (page 18, line 31-page 19, line 2). Serhan et al. states at page 19, lines 25-26 of the disclosure a therapeutically effective amount of an anti-inflammatory of the invention from 0.1 to 20 mg/kg.

Present claim 1 recites the limitation of "an amount effective to reduce subclinical inflammation" in line 3 of the claim. The Examiner considers this limitation to be directly anticipated by the teachings of Serhan et al., who teaches the use of a therapeutically effective amount sufficient to diminish inflammation (see page 18, line 31-page 19, line 2).

Present claim 5 recites that the amount of DHA may be administered substantially contemporaneously with a second medicament. Serhan et al. teaches a method of treatment using a combination of an omega-3 fatty acid, such as DHA, in combination with aspirin. Absent factual evidence to the contrary, the teachings of the reference, which state that the "combination of an omega-3…fatty acid and aspirin" are to be administered, are indicative of

essentially simultaneous administration. Serhan et al. further discloses the use of a "single bolus" administration at page 19, lines 13-15, indicating that the composition may be administered as a single dose. Furthermore, Serhan et al. also teaches that they may be administered at two different times (see also page 19, lines 13-15). Although Serhan et al. is silent as to a specific timeframe within which administration of the two components of the active composition must be administered, the Examiner considers the teachings of Serhan et al. to anticipate the claim limitation of "substantially contemporaneously" as recited in present claim 5.

Present claim 5 also recites "an amount sufficient to reduce circulating C reactive protein in the patient" (see lines 3-4 of claim 5). Applicant has disclosed in the present specification that DHA may be administered in a high dose, or "greater than 200 mg/day" and in a preferred embodiment, "greater than 1.5 g/day" (see Applicant's acknowledgement, page 15, paragraph [050], lines 4-11). Serhan et al. expressly teaches an amount of an anti-inflammatory compound of the invention to be used in a dosage of 0.1 to 20 mg/kg. Thus, for an average 70 kg adult human, the dose range taught by the reference would have been between 7 and 1400 mg, and since the reference indicates that the compounds may be administered as a single dose (see page 19, lines 13-15), this is indicative of a dose of 7 to 1400 mg/day. Therefore, although Serhan et al. does not expressly teach a dose range of 200 mg/day to 1.5 g/day, the dose range of the reference and the dose range underlying the recitation "an amount sufficient to reduce circulating C reactive protein in the patient" clearly overlap insofar as the present claim reads on 200 mg-1400 mg/day and is considered to be anticipated by Serhan et al.

Because the teachings of Serhan et al. state the use of "a therapeutically effective amount of an anti-inflammatory of the invention is 0.1-20 mg/kg" (page 19, lines 25-26), the Examiner considers this disclosure to teach a dose of 0.1-20 mg/kg of either the anti-inflammatory compound DHA **or** the anti-inflammatory compound aspirin. Thus, as stated above, for an average 70 kg adult human, the dose range taught by Serhan et al. would have been between 7 and 1400 mg. Since the reference teaches that the compounds may be administered as a single dose (see page 19, lines 13-15), this is indicative of a dose of 7 to 1400 mg/day. Present claim 9 recites a dose of aspirin from 35-250 mg/day, which clearly lies within the range taught by Serhan et al. and is, thus, considered to be anticipated. Furthermore, present claim 21 recites the use of DHA at a dose of 200-500 mg/day and the use of aspirin at a dose of 81 to 162 mg/day. Both the dose range of DHA **and** the dose range of aspirin clearly lie within the range of 7 to 1400 mg taught by Serhan et al. (see above) for either anti-inflammatory compound of the invention and, thus, claim 21 is considered to be anticipated. See MPEP §2131.01 regarding rejections under 35 U.S.C. 102 for ranges.

Furthermore, it is recognized that the prior art teachings of Serhan et al. do not expressly recite that the amount of DHA administered with a second medicament, in this case, aspirin, is an amount sufficient to reduce circulating C reactive protein in the patient, but the reference does, however, teach a method of treating the inflammatory conditions of arterial inflammation, arthritis, cardiovascular diseases (page 11, lines 18-20), spasmogenic conditions, such as cerebral spasm or stroke (page 22, lines 18-25), conditions involving blood platelet aggregation, such as

thrombosis, strokes having a total or partial thrombotic origin or coronary thrombosis (page 22, line 30-page 23, line 2), and inflammatory conditions of the heart, such as coronary infarct damage or smooth muscle proliferation disorders, such as restenosis following angioplasty (page 23, lines 22-25), using a combination of DHA and aspirin at a dose range that clearly overlaps that of the present disclosure (see second paragraph, page 20 of the present Office Action). However, because the particular method steps and compounds that are present in the instant claims are also in the patent, it is deemed that the C reactive protein reduction properties of the amount of the compound of the prior art used to treat the above-mentioned conditions would have been inherent, whether recognized by the patentees or not. The claiming of a new use, new function or **unknown property** that is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 U.S.P.Q. 430, 433 (CCPA 1977). See also MPEP §2112. It is irrelevant that the prior art observers did not recognize the property or function of the disputed claims; if the prior art inherently possesses that characteristic, it anticipates. Applicant's attention is further drawn to the MPEP at §2113, which states, "As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). Thus, claim 5 is properly rejected as being anticipated by Serhan et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I Claims 1-3, 5-9, 14-15 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Serhan et al. (International Publication No. WO 01/60778 A2; 2001), for the reasons recited above in Section Heading III of "Claim Rejections-35 U.S.C. 102", in view of Cecil's Textbook of Medicine (21st Edition, Volume 2; p. 2105-2106) and Minchoff et al. ("Syndrome X. Recognition and Management of this Metabolic Disorder in Primary Care", 1996, abstract).

The differences between the Serhan et al. reference and the presently claimed subject matter lie in that the reference does not teach:

(i) the use of DHA/aspirin in patients suffering from type 2 diabetes mellitus, metabolic syndrome or hypertension; and

(ii) the method of assessment for stroke and treatment with DHA/aspirin as recited in present claims 14-15.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) Serhan et al. broadly discloses a method of treating inflammatory disorders, especially cerebrovascular and cardiovascular diseases, using a combination therapy of DHA and aspirin, but does not expressly teach the use of such a therapy in patients suffering from type 2 diabetes mellitus, metabolic syndrome or hypertension. However, it was well known in the art that such conditions were known risk factors for the development of stroke (see Cecil's Textbook of Medicine, p.2105, especially Table 470-3). Thus, it would have been reasonably suggested that the treatment of stroke in a patient using a combination therapy of DHA/aspirin would concurrently be treating a patient suffering from type 2 diabetes mellitus or hypertension, since it was known in the art that these conditions contribute to the development of stroke. Although Cecil's Textbook is silent as to the contribution of metabolic syndrome as a risk factor for stroke, syndrome X was known in the art to be associated with insulin resistance and is linked to non-insulin dependent diabetes mellitus (see abstract of Minchoff et al.), which is indicative that a condition such as Syndrome X with a similar effect on insulin tolerance would also have been

reasonably expected to contribute to the development of stroke in essentially the same manner as diabetes mellitus.

(ii) As stated above, the broad disclosure of Serhan et al. teaches a method of treating inflammatory disorders, especially cerebrovascular and cardiovascular diseases, using a combination therapy of DHA and aspirin. However, Serhan et al. does not expressly state a method of treating a patient at risk for developing stroke by assessing the following risk factors and then subsequently administering DHA/aspirin combination therapy: abdominal obesity, high triglycerides, low HDL cholesterol, high blood pressure, small LDL particle size, high fasting glucose and elevated levels of C-reactive protein, as recited in present claim 14. However, conditions such as hypertension, diabetes mellitus, obesity, atherosclerosis, coronary artery disease or asymptomatic carotid stenosis were known in the art to be risk factors associated with the development of stroke (see Cecil's Textbook of Medicine, p.2105-2106). The treatment of patients with any pharmaceutical therapy targeted at reducing the risk of developing stroke, whether it be a pharmaceutical therapy well known in the art or the presently claimed active composition, would necessarily indicate a medical assessment of the risk factors or conditions known to contribute to the development of stroke prior to treatment by a medical professional. Such a person would not only be motivated to do so in order to identify those patients that would benefit significantly from the administration of such a treatment, but also to determine the degree of risk and how aggressive the therapeutic regimen would need to be. Furthermore, variations within any one or more of these risk factors, in combination with any number of other variable factors, such as age, gender, sex, race, lifestyle, alcohol consumption or the presence of other

concurrent diseases or disorders, would be reasonably expected to differ from patient to patient, and thus, the determination of the threshold levels for what would constitute a patient "at risk" and a normal patient would have been a determination well within the purview of the skilled artisan.

Conclusion

Rejection of claims 1-9, 14-15 and 21 is deemed proper.

Claims 10-13 and 16-20 have not been treated on the merits due to improper multiple dependency.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The Examiner can normally be reached on Monday-Friday (8:30 AM-6:00 PM), alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low can be reached on (571)-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 7, 2005

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